
miR-294/miR-302 Promotes Proliferation, Suppresses G1-S Restriction Point, and Inhibits ESC Differentiation through Separable Mechanisms.

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Public Summary:

Scientific Abstract:

The miR-294 and miR-302 microRNAs promote the abbreviated G1 phase of the embryonic stem cell (ESC) cell cycle and suppress differentiation induced by let-7. Here, we evaluated the role of the retinoblastoma (Rb) family proteins in these settings. Under normal growth conditions, miR-294 promoted the rapid G1-S transition independent of the Rb family. In contrast, miR-302 suppressed the further accumulation of cells in G1 in response to nutrient deprivation and cell-cell contact in an Rb-dependent fashion. We uncovered five additional miRNAs (miR-26a, miR-99b, miR-193, miR-199a-5p, and miR-218) that silenced ESC self-renewal in the absence of other miRNAs, all of which were antagonized by miR-294 and miR-302. Four of the six differentiation-inducing miRNAs induced an Rb-dependent G1 accumulation. However, all six still silenced self-renewal in the absence of the Rb proteins. These results show that the miR-294/miR-302 family acts through Rb-dependent and -independent pathways to regulate the G1 restriction point and the silencing of self-renewal, respectively.

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